REMARKS/ARGUMENTS

Reconsideration of the present application, as amended, is respectfully requested.

A. CLAIM AMENDMENTS

As a result of the present amendment, claims 1-7, 9-10, 13, 16 and 36-38 are presented in the case for continued prosecution. Claim 1 has been amended to clarify conjugation of a polyalkylene oxide to the sugar amino group $NR_{11}H$ of a vancomycin. Claims 2-4 and 7 as amended now include the polyalkylene oxide originally recited in claim 8. Claim 8 has been cancelled without prejudice. New claims 36-38 are added to more particularly set forth that which Applicants consider to be their invention. Support can be found, for example, in paragraph [0026] of the specification for claim 36 and paragraph [0027] for claims 37-38. No new matter has been added.

B. SUMMARY OF THE INVENTION

The present invention provides methods of preparing vancomycine-polyalkylene oxide conjugates under reaction conditions which favor conjugating the polyalkylene oxide to the sugar amine group of the vancomycin among nine (9) amine groups of vancomycin. The reaction conditions include at least about a ten-fold molar excess of triethylamine (TEA) and a sufficient amount of dimethylformamide (DMF). One of preferred reaction conditions includes at least about 20-fold, more preferably at least about 30-fold molar excess TEA. The vancomycin-polymer conjugates prepared according to the claimed methods are homogenous. The claimed methods are advantageous to provide homogenous prodrugs which can have uniform, more predictable pharmacokinetic profiles including therapeutic effects.

C. CLAIM REJECTIONS UNDER 35 USC §112, FIRST PARAGRAPH

At pages 3-7 of the Office Action, claims 1-10, 13 and 16 are rejected under 35 U.S.C. §112, first paragraph, allegedly failing to comply with the written description requirement.

The Examiner has taken the position that there are insufficient descriptions for recitations of "a polymer residue containing at least one leaving group" that would react with the amine group of vancomycin. The Examiner also indicated that there are nine (9) amine groups in vancomycin. The Examiner further indicated that there lacks written description of "polymer residue",

"bifunctional linker" and "sufficient amount of reactants".

1. "polymer residue containing at least one leaving group" and "polymer residue":

In response to the Examiner's note on the "polymer residue containing at least one leaving group" and "polymer residue", while not admitting the Examiner's position, Applicants have amended claim 1 to recite "polyalkylene oxide residue containing at least one leaving group". Contrary to the Examiner's position, paragraphs [0028]-[0037] of the specification describe various polymeric residues with at least one leaving group which artisans can appreciate without undue experimentation. Suitable leaving groups employed in the activated polymer are listed particularly on page 20, paragraph [0033], lines 2-5. In addition, claim 1 as amended now clarifies that the sugar amine group $NR_{11}H$ of vancomycin reacts to conjugate to a polyalkylene oxide.

According to the Examiner, there would be at least nine different vancomycin-polymer conjugates prepared since vancomycin has nine different amine groups which would react with an activated polymer. In contrast to the Examiner's position, the reaction conditions claimed herein allow preparing homogenous vancomycin-polymer conjugates. The sugar amine group, $NR_{11}H$ of vancomycin among the nine alleged amine groups forms a conjugate with the polymer under reaction conditions recited in claim 1. The reaction conditions including a ten-fold molar excess of triethylamine (TEA) and a sufficient amount of dimethylformamide (DMF) allow site specific conjugation substantially exclusively to the sugar amine group, $NR_{11}H$ of vancomycin. See paragraphs [0025]-[0026] of the specification. For example, compounds **2, 4, 12, 21, 29** and **45-46** are particular embodiments of polymers with leaving groups which can be employed in the claimed methods. The polyalkylene oxide polymers with various bifunctional linkers and leaving groups described in the specification can conjugate to the sugar amine group of the vancomycin under the claimed reaction conditions. For example, see compounds **3, 5, 13, 22, 30, 47** and **49.** See also Examples 1, 2, 8, 16, 21 and 32-33 of the specification. In light of the sufficient disclosure and knowledge of artisans in the art, it is urged that the written description requirement concerning the recitation of polyalkylene oxide residue containing at least one leaving group as amended herein is met.

2. "sufficient amount of reactants":

Concerning the Examiner's note on the "sufficient amount of reactants", Applicants respectfully disagree.

Applicants assume that the Examiner's note on "sufficient amount of reactants" refers to the recitation of "sufficient amount of dimethylformaide" in claim 1. Applicants request the Examiner's clarification regarding the "sufficient amount of reactants". The sufficient amount means an amount capable of dissolving reactants such as vancomycin. See paragraph [0027] of the specification. For example, the amount of DMF can range from about 10 mg/g to about 500 mg/g based upon the vancomycin used. The meaning in the disclosure is also consistent with what artisans in the art appreciate. Accordingly, it is urged that the written description requirement concerning the recitation of "sufficient amount of DMF" is met.

3. "bifunctional linker":

Concerning the Examiner's note on the "bifunctional linker", Applicants respectfully disagree.

The bifunctional linker is a moiety having one end which can bind to the polyalkylene oxide residue and the other end which can link to the vancomycin. Artisans in the art can appreciate suitable linkers for forming the vancomycin-polymer conjugates without undue experimentation. In contrast to the Examiner's position, suitable bifunctional linkers are described in paragraph [0029] of the specification. When the optional bifunctional linker is present, it covalently links the polyalkylene oxide to aromatic systems for eventual releasable attachment to vancomycin. Thus, various bifunctional linkers employed in polyalkylene oxide polymers containing at least one leaving group can be appreciated by artisans in light of the disclosure and knowledge of artisans in the art.

For all of the above reasons, it is urged that the written description requirement is met. Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. §112, first paragraph, is respectfully requested.

D. REJECTIONS UNDER 35 U.S.C. §102(a) and (e)

The Examiner rejected the subject matter of claim 1 as being anticipated under 35 U.S.C. §102(a) and (e) by Martinez, et al. (US Patent No. 6,395,266). The Examiner indicated that the '266 patent discloses conjugating vancomycin to a polymer via amine. The Examiner has taken the position that the recited reaction condition in claim 1 of being "capable of reacting with the sugar amine group of said vancomycin compound in the presence of at least about a ten-fold molar excess of triethylamine and a sufficient amount of dimethylformamide" is not an active step. The Examiner further indicated that the active step is the coupling of vancomycin with a polymer residue containing at least one leaving group. Applicants respectfully disagree.

Applicants call attention to the requirement that a rejection under 35 U.S.C. §102 requires that all of the elements of the rejected claims be found within the cited reference. The '266 patent is, however, silent with regard to the reaction conditions necessary for the sugar amine-specific attachment to vancomycin. The reaction conditions for the site-specific substitution include at least a ten-fold molar excess of TEA and a sufficient amount of DMF. See paragraphs [0025]-[0027] of the specification.

Moreover, contrary to the Examiner's position, the reaction condition recited in claim 1 is essential to allow the particular sugar amine group, $NR_{11}H$ at V_3 position, not other random amine groups, of vancomycin to conjugate to the polymer. Unlike the claimed methods, the methods according to Martinez et al. do not provide sugar amine specific, homogenous conjugation of vancomycin to the polyalkylene oxide polymer.

Accordingly, it is respectfully urged that claim 1 is not anticipated by the '266 patent. Reconsideration and removal of the rejection is respectfully requested.

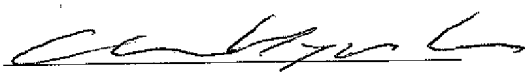
E. FEES

This response is being filed within the shortened period for response. Thus, no further fees are believed to be required. If, on the other hand, it is determined that any further fees are due or any overpayment has been made, the Assistant Commissioner is hereby authorized to debit or credit such sum to Deposit Account No. 02-2275.

Pursuant to 37 C.F.R. 1.136(a)(3), please treat this and any concurrent or future reply in this application that requires a petition for an extension of time for its timely submission as incorporating a petition for extension of time for the appropriate length of time. The fee associated therewith is to be charged to Deposit Account No. 02-2275.

An early and favorable action on the merits is earnestly solicited.

Respectfully submitted,
LUCAS & MERCANTI, LLP



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